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WORKING DRAFT

RESPONSE TO HEW REPORT

Prepared By

Ad Hoc Committee

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RESPONSE TO HEW REPORT TO CONGRESS ON SMOKING AND HEALTH AND SURGEON GENERAL'S REPORT ON THE HEALTH CONSEQUENCES OF SMOKING--1967

I. Generally.

A. The Secretary's Report.

Pursuant to the Federal Cigarette Labeling and Advertising Act of 1965, Secretary Gardner has submitted a report to Congress concerning "current information on the health consequences of smoking" and "recommendations for legislation". The Secretary reports that the "principal thrust" of more than 2,000 recent research studies completed and reported in "the biomedical literature" has been to "strengthen the conclusions reached in 1964 and to determine more precisely the extent of death and disability attributable to cigarette smoking."*

*Compare the words "attributable to" with the more careful wording in mortality and morbidity reports showing deaths and disabilities statistically "associated" with cigarette smoking: (1) The Division of Vital Statistics, in listing deaths from diseases statistically associated with smoking, warned that it had "no information" as to the proportion "actually caused" by smoking (HEW Appropriations Hearings, 1968, Part 4, p. 79); and (2) The National Center for Health Statistics pamphlet on "Cigarette Smoking and Health Characteristics," which presents statistics on disability, observed that data showing a statistical association "cannot establish any existing relationship as a causal one" (p. 6). When asked (see page 78 of the same volume on the HEW Hearings) why he referred to "at least 125,000 premature deaths, and maybe as many as 300,000 deaths . . . due to cigarette smoking", Surgeon General Stewart responded, "Did I say 'due to'?" See Appendix A and the discussion at pages 10 and 18.

The Secretary further reports (1) that the present warning label on cigarette packages "is inadequate"; (2) that the label has not been a significant deterrent to cigarette smoking ("as amply shown in the recent report of the Federal Trade Commission") and "does not have any impact on the many children and young people who are daily exposed to cigarette advertising"; and (3) that "the accumulated evidence strongly suggests that the lower the 'tar' and nicotine content of cigarette smoke, the lower the harmful effect" and that information concerning content "of the smoke of each brand of cigarettes should be put before the smoker and the potential smoker" so the consumer would "thus be able to make an informed choice of product".

The Secretary, based on the considerations stated, recommends (1) that the warning label on each package of cigarettes be "strengthened to state more specifically and positively that cigarette smoking is a hazard to health"; (2) that the warning should be required in advertisements as well as on cigarette packages; and (3) that both the label and advertising should be required to contain information on the "tar" and nicotine levels "in the smoke of the cigarette" and the identity and quantity of such other substances or agents in the smoke as may subsequently be found by the

appropriate Federal agency to contribute to the health hazards of smoking.

The Secretary attached a "Surgeon General's summary report", said to contain "detailed information on the health consequences of smoking", and referred to technical information, not attached, which "will be available as an addendum to the Surgeon General's Report".

This response will demonstrate that "the gaps in knowledge identified in 1964"* in Smoking and Health still exist, particularly with respect to "the mechanism by which ingredients in cigarette smoke induce harmful effects on the human body"* if, in fact, they do.

Until a "mechanism" has been identified, it is premature to assign a causative role to cigarette smoking with respect to any disease and meaningless to speak in terms of "how much illness and mortality would be averted by cessation of smoking".* It is equally meaningless to modify the warning label imposed by Congress in 1965 unless some scientific breakthrough has implicated cigarette

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*Secretary Gardner's statement, page 1.

smoking by producing evidence far more persuasive than that presented in the Surgeon General's 1967 report. In this respect it is certainly significant that the Secretary's statement, in dealing with the additional research efforts since 1964 refers in detail only to "epidemiological information"--as to which the Surgeon General's Advisory Committee had this to say: "Statistical methods cannot establish proof of a causal relationship in an association" (Smoking and Health, p.20).

The Secretary's recommendation that a warning be placed on cigarette advertising refers to "the recent report of the Federal Trade Commission". Since no data or other material supporting such a recommendation is incorporated in the HEW report, it will not be dealt with further in this response.

The Secretary advances no reason why or how "tar", which presented "a puzzling anomaly" (Smoking and Health, p. 33) in 1964, had suddenly become an indicator that would enable a smoker to make "an informed choice". Equally mysterious is the conclusion that the lower the nicotine content of cigarette smoke, "the lower the harmful effect". If the "principal thrust" of recent studies has been to "strengthen the conclusions reached in 1964", then one

of the conclusions "strengthened" is the following:

> "(T)he chronic toxicity of nicotine in quantities absorbed from smoking and other methods of tobacco use is very low and probably does not represent an important health hazard." (Smoking and Health, p. 32)

The "tar" and nicotine recommendation is discussed hereafter commencing at page 11.

B. The Surgeon General's Report--1967.

The 1967 report discusses generally current information on the health consequences of smoking and then presents "the major findings of research studies published in the past three to four years" under the following six headings:

1. Smoking and Overall Mortality.
2. Smoking and Overall Morbidity.
3. Smoking and Cardiovascular Diseases.
4. Smoking and Chronic Bronchopulmonary Diseases (Non-Neoplastic).
5. Smoking and Cancer.
6. Other Conditions and Research Areas.

The introductory portion of the Surgeon General's 1967 report refers to earlier deaths and excess disability which "would not have occurred if those affected had never smoked" and attributes practically all of the earlier deaths from lung cancer, a substantial portion of the earlier deaths from chronic bronchopulmonary diseases and a portion of the earlier deaths of cardiovascular origin to cigarette smoking. The report observed that the conclusion that cigarette smokers have higher death rates than the

nonsmoking counterparts has "changed the emphasis of the present problem away from the question 'Does cigarette smoking cause disease?'" to more precise questions dealing with the degree of association, the portion of early mortality and excess disability caused by smoking, the portion that could be averted by the cessation or reduction of cigarette smoking and (in fourth and last place on the Surgeon General's list) "What are the biomechanisms whereby these effects take place and what are the critical factors in these mechanisms?"

The "changed emphasis" away from the question of whether cigarette smoking causes disease and the placing of determination of biomechanisms in last place is proof that what many scientists who appeared before Congress in 1965 feared would happen has happened. An official position that cigarette smoking causes disease has been taken and the primary mission of much "research" is to show additional statistical "associations" between cigarette smoking and certain diseases rather than to discover the basic biomechanisms actually responsible for such diseases. In this regard, a recent publication listing "ongoing research" in the cigarette-health field reveals that a substantial part of the basic research

being done today is tobacco industry financed and administered either by the American Medical Association or the Council for Tobacco Research (through its independent Scientific Advisory Board); and that a substantial amount of Government supported "research" (over 1/3 of the total number of projects listed) consists of "behavioral" studies, educational programs and anti-smoking propaganda. A review of the footnotes to the 1967 Surgeon General's summary report discloses no reference to any research demonstrating a "mechanism" by which smoking is proved to cause any human disease.* The references cited consist of the 1964 Surgeon General's Report, an unpublished smoking and health bibliography, two reports on mouse painting, fifteen statistical surveys and a report on cigarette smoking "patterns".

The "gaps" in the case against cigarettes which were pointed out after the 1964 Surgeon General's report still exist. Nothing contained in the 1967 summary report has eliminated or lessened them. Some of the material contained in the report, and considerable material which was not incorporated therein, supports

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*Smoking itself cannot be <u>the</u> cause of any disease since non-smokers develop all of the diseases statistically associated with smoking.

"highlights" such as the following rather than those selected by the Surgeon General:

> Several recent studies show no association between cardiovascular disease and cigarette smoking. The "consistent association" referred to in the Surgeon General's report in 1964 is no longer "consistent". Furthermore the recent literature contains strong evidence that cardiovascular disease is multifactorial in origin and that constitutional factors play a significant role in its cause.
>
> The epidemiological data from which the association between lung cancer and cigarette smoking has been derived has been thrown into question by recent large scale studies showing no association.
>
> Scientists have failed to discover any ingredient in cigarette smoke responsible for disease in man and no mechanism by which any human disease is caused by cigarette smoking has been demonstrated.

These and other observations are discussed in more detail in the following sections.

II. Specific Areas

A. Smoking and Overall Mortality.

"The primary addition to knowledge in the areas of smoking and overall mortality comes from the four major population studies", says the 1967 report. The "addition", for the most part, is simply a repetition of similar material included in the 1964 report.

Without specifying how much, the 1967 report states (p. 20) that "much of the excess" mortality would not have occurred "if it had not been for cigarette smoking". The report does not say, however, what the method of identification was nor how many deaths would properly be included. It does concede, with respect to the "remainder" that some of the excess deaths "would have occurred anyhow". Appendix A reviews some of the more inflammatory statements made about "excess deaths" and demonstrates a six hundred percent overstatement even if the 1964 Surgeon General's findings of causation (cancer of the lung and larynx, and bronchitis only) were accepted.

1. Measures of Exposure

For some reason the Surgeon General has included the section on "measures of exposure" in the section on mortality. This section discusses, for the most part, a paper written by Dr. Daniel Horn and others (12)* which attempted to define current smoking patterns. The measures surveyed included average number of cigarettes smoked per day, the "tar" rating of the brand smoked, the portion of the cigarette smoked, and questions (which would clearly mean different things to different people**) on both depth and frequency of inhalation. The report observes, at page 21, that "there are many individuals with high exposure on one measure but low exposure on another." Although Dr. Horn concluded in his paper that

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*These and similar numbers in parentheses refer to the bibliography of cited references in the Surgeon General's 1967 report.

**"In this study inhalation was looked at in terms of two basic dimensions, depth and frequency. They were ascertained by the following two questions:

1. 'When you now smoke cigarettes, how deeply do you usually draw in the smoke? Would you say: As deeply into the chest as possible, only partly into the chest, as far back as the throat, well back into the mouth, or just puff and don't really draw it in at all?'

2. 'Do you usually: Inhale almost every puff of each cigarette, inhale a few puffs of each cigarette, inhale a few puffs of some cigarettes, or do you not inhale at all?'"

smokers who smoke only a few cigarettes may consume more of these cigarettes than persons who smoke more and that no "toleration" levels have been established for human health purposes, the 1967 report concludes (without citing any evidence whatsoever) that the "existence of a dose-response relationship between exposure to cigarette smoke and the risks most clearly associated with cigarette smoking is now generally accepted". This conclusion is also in conflict with the data indicating that inhalation may be immaterial or even negatively associated with "risk". See Smoking and Health, 188, and (7) in the 1967 report ("Bronchial Cancer and Tobacco", R. Doll).

The 1967 report next cites some work reported by Wynder and Hoffman in October, 1963. The Surgeon General states:

> "Wynder and Hoffman (20) have shown in laboratory experiments with animals that the tumorigenicity of cigarette smoke can be reduced by alteration in the cigarette which reduces the 'tar' and nicotine content. They use the term 'indicator' for 'tar' and nicotine content (the two measures tend to be used jointly since when one is high the other tends to be high unless the nicotine has been removed in processing), or other measures which reflect this type of relationship lacking the identification of specific agents which are responsible for the effect."

"The purpose of laboratory studies" involving tobacco smoke condensate, said Wynder and Hoffman, "was not to establish cancer causation for man", but to determine if such condensate is carcinogenic to animal tissue and, if so, which constituents are primarily responsible for its "tumorigenic activity".

Wynder added copper nitrate and nickel acetate to standard tobacco and reported that such tobacco "yielded a condensate which produced significantly less tumorigenic activity than standard tobacco smoke condensate." He conceded that the "additives are not practical" but that the studies "add to our understanding of the formation of these components" (apparently benzo(a)pyrene and phenols).

The article discusses the varying content of benzo(a) pyrene and phenols in different type of tobacco and seems to imply that these are constituents "which at least in part may account for the tumorigenic activity" in animal tissue. (In this regard, a more recent report negates any significant effect of benzo(a) pyrene--see Section E, "Smoking and Cancer".)

The authors reaffirm in their summary that if the "results are applied to the human setting, caution must be used" and do not suggest, as the Surgeon General claims at page 22 that

"tumorigenicity of cigarette smoke" can be reduced by reducing the "tar" and nicotine content. As a matter of fact, quantitative reduction was not even discussed and the authors did not link nicotine to carcinogenic activity, consider it an "indicator" or even comment on it.

A 1965 study by Bock, Moore and Clark (2) was cited to "show a similar variation in carcinogenic activity of tobacco 'tar' obtained from different types of cigarettes." It is not noted in the Surgeon General's report that Bock, et al., found that removal of the nicotine made no difference whatsoever with respect to tumorigenicity, learned that the mice developed a number of "spontaneous" pulmonary adenomas unrelated to the treatment and concluded that the same amount of "tar" from English cigarettes was much more "potent" than from American cigarettes. The 1967 report states, "The preponderance of scientific evidence strongly suggests that the "tar" and nicotine content of cigarette smoke is a meaningful factor in the measurement of dosage." This is an amazing statement if the articles cited are suppose to support it. The Horn study was simply a survey of smoking habits. The Wynder and Bock articles reported on mouse painting experiments. These experiments, in which

the back of the mouse is shaved and then periodically subjected to applications of artificially derived condensate of cigarette smoke, may be described as employing the wrong material in the wrong form and the wrong concentration upon the wrong tissue of the wrong animal. It has been said that the only way a man could get the same concentration over the area of the lung would be to smoke a hundred thousand cigarettes a day.

2. Cessation of Smoking

The heading "Smoking and Overall Mortality" also contains a subhead, "Cessation of Smoking." This is called "an extreme example of the reduction of dosage".

With respect to the "overall reduction" reported among British physicians it is extremely interesting to note that the British physicians had a much more favorable lung cancer death rate even when they smoked about the same amount as the general population, and that the overall decline cannot be attributed to any improvement of risk among former smokers (". . . the actual results suggest that the risk for acquiring the disease remains almost the same as it was when smoking was discontinued . . ."). The decline

may be explained by some of the studies which report less lung cancer among the well-to-do and to the probability that diagnosis among British physicians has been much better than among the population generally (which could account for some of the continuing "increase" in the non-physician population) In any event, it would be most interesting to see additional data with respect to the age brackets covered by the survey, the percentage of non-response, etc., particularly in view of the limited number of confirmed lung cancer cases reported (277) and the anomalies in Doll's articles showing a high association of lung cancer with pipe and cigar smokers and higher rates among cigarette smokers who do not inhale.

The 1967 report concedes that data showing a reduction in mortality has been somewhat obscured by the fact that ill health is a frequent cause of giving up smoking "so that death rates and disability rates for ex-smokers as a group tend to be high for an initial period of time following cessation." (Compare this with the Doll article on British doctors which reports a greater improvement in death rates from lung cancer during the initial period studied.) As a matter of fact, death rates for ex-smokers in some instances are higher than for people who continue to smoke (Smoking

and Health, p. 93). On the other hand, some ex-smokers have been found to have less heart disease than persons who had never smoked. This was attributed by Dr. Daniel Horn to the probability that they were sufficiently concerned with their own health "to maintain proper dietary habits and adequate exercise, and thereby have a lower death rate." (Cigarette Labeling Hearings, House of Representatives, 1965)

B. Smoking and Overall Morbidity.

This section is based almost entirely on the National Health Survey, "Cigarette Smoking and Health Characteristics". Significantly this report specifically concedes that the statistical associations found cannot prove any causal relationship between cigarette smoking and any chronic condition (p. 6). It should also be observed that with the exception of chronic bronchitis (which may or may not have been confused by persons interviewed with a simple cough) none of the conditions mentioned have been found to be causally related in any way with cigarette smoking. This survey is reviewed in connection with some of the disease entities discussed hereafter and in some detail in Appendix B.

there being no accepted definition of bronchitis

C. Smoking and Cardiovascular Disease

1. Introduction

In 1964, the Advisory Committee to the Surgeon General of the Public Health Service concluded:

> "Male cigarette smokers have a higher death rate from coronary artery disease than nonsmoking males, but it is not clear that the association has causal significance." (P. 327)

The Committee also found that the association between cigarette smoking and other cardiovascular disorders* "is less well established" (P. 327).

Significantly, the Committee did not assert that smoking causes coronary artery disease.** Furthermore, the Committee acknowledged that "other facts such as high blood pressure, high serum cholesterol and excessive obesity" were associated with "an unusually high death rate from coronary disease." (P. 327)

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*"Other cardiovascular disorders" include miscellaneous circulatory diseases including other heart diseases, hypertensive heart disease, and general arteriosclerosis.

**"Coronary Artery Disease " is sometimes called "Coronary Heart Disease" or "coronary disease."

Moreover, the Committee conceded that "the basic cause or causes of coronary heart disease are obscure."

In spite of the additional evidence that he alleges has accumulated in the intervening years, the Surgeon General did not arrive at any different conclusions with regard to the etiology of cardiovascular disease than the Advisory Committee did in 1964. In his 1967 Report, the Surgeon General did not assert that cigarette smoking is a cause of any cardiovascular disease. (Pp. 41-42)

2. Summary

The "highlights" of the cardiovascular disease section are, by and large, overstated and assailable. Certainly they are not borne out by the studies cited nor by the data outside the 1967 report. Presumably they are based on the nine cited articles and several articles to which no reference is made in the limited bibliography at the end of the report. The report, after stating that 2,000 additional articles on smoking and health had been published since 1964, omits numerous articles which do not support its conclusions. or are at variance with them

Perhaps the most significant article to appear on

coronary heart disease since 1964 is the article by Lundman (14). In addition, the work of Cederlof (4, 5 and 6) on angina pectoris* is highly significant. Yet, although both studies are cited in another section of the report, neither is either discussed or mentioned by the Surgeon General in connection with this subject.

Contrary to the "highlights" in cardiovascular section, the following are more appropriate conclusions based upon the material published regarding cardiovascular disease since the publication of Surgeon General's report in January 1964:

1. The association between cigarette smoking and coronary heart disease that was found by the Surgeon General's Advisory Committee in prospective and retrospective epidemiological studies is less clear today after more such studies have failed to find the alleged association.

2. Additional information has been published indicating that the cause or causes of coronary heart disease and other cardiovascular diseases are multifactorial.

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*Sudden, intense and recurring short pains in the chest

3. As the evidence of a multifactorial etiology in coronary heart disease has developed, new methods of analyses using sophisticated computer technology have raised questions about the essentially univariate prospective mortality studies conducted in the years prior to the publication of the Surgeon General's report.

4. Recent studies have tended to confirm that constitutional factors enter into the etiology of coronary heart disease. Publications have cited stress as a possible factor in coronary heart disease and "way of life" is being studied as another factor.

5. Evidence showing any mechanism by which cigarette smoking causes coronary heart disease has not been forthcoming.

3. <u>The Status According to the Surgeon General</u>

The section on smoking and cardiovascular disease (pp. 37-42) includes nine citations, six of which are to the four mortality surveys already discussed in the previous section. A seventh citation is to a longitudinal study of San Francisco longshoremen, and the last two are to pamphlets in the Vital and Health Statistics Series (17, 18).

a. Prospective Mortality Studies

In the four major prospective studies about which data has been published since the issuance of Smoking and Health, there are inconsistencies which raise puzzling problems for the epidemiologist. All four of these studies were reported in some detail in Smoking and Health and therefore the recent reports on them are, for the most part, describing "old" rather than"new" data.

For instance, the Doll and Hill study found an association for men between cigarette smoking and only that portion of cardiovascular disease denominated "coronary disease without hypertension." By contrast, they found no relationship among women between cigarette smoking and cardiovascular disease. In fact, the death rate for women for continuing smokers was less than that for nonsmokers which, in turn, was less than that for former smokers. Thus, according to these figures, the risk of dying from coronary disease for females was greater for the nonsmoker than for the cigarette smoker, and, once a woman commences cigarette smoking, her risk of dying of the disease is even greater if she ceases than it is if she continues. This would seem to contradict a theory that, among women, coronary

disease is caused by cigarette smoking. Furthermore, the nonsmoking woman appears to have a three times higher risk of dying from "coronary disease without hypertension" than the woman who smokes one to fourteen cigarettes per day.

In the Doll and Hill study, the effect of inhalation was studied. According to the Surgeon General's 1964 Report, "at each level of consumption the [mortality] ratio increases with the amount of inhalation reported by the smokers." (P. 324) Nonetheless, in the Doll and Hill study, the death rate for "coronary disease without hypertension" for continuing smokers who inhale was only slightly different from the death rate for continuing smokers who do not inhale. Thus, according to this information, it made little difference whether the continuing cigarette smoker did or did not inhale.

In the Hammond study, the mortality ratio from cerebrovascular lesions for men 75 to 84 years of age for cigarettes only was less than that for nonsmokers. If such ratios are to be believed, once a person attains the age of 75, he should consider taking up cigarette smoking in order to increase his chances of not suffering death from cerebrovascular lesion.

b. Longshoremen Study

In addition to the four major mortality surveys, the Surgeon General referred in his 1967 Report to the study of San Francisco longshoremen (3). In this ten year follow-up of 3,994 longshoremen, the authors of this study found that, for age 35 to 44, the death rate of the nonsmoker was three times that of the smoker. At older ages, however, the death rates of the nonsmokers were lower than those of the smokers.

The authors of the longshoremen study admitted that no known mechanism existed to explain the statistical association between smoking and coronary heart disease. The authors concede that:

> "We do not know the etiology of many of the chronic diseases, such as coronary heart disease."

In a later study, the authors reported on their longitudinal study of blood pressure among the longshoremen. They stated that their data supports the concept that hypertension and blood pressure are the result of multifactorial genetic traits. They acknowledged that their blood pressure data casts some doubt on the simple statistical association between coronary heart disease and cigarette smoking.